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ORIGINAL ARTICLES

CLINICAL STUDIES IN CUTANEOUS ASPECTS OF TUBERCULOSIS.

II. THE DIAGNOSTIC AND CLINICAL RELATIONS OF CERTAIN TUBERCULIDS.

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THE tuberculid is a cutaneous lesion of exceptional interest to the pathologist, the internist and the general diagnostician. The term was devised by Darier to describe a group of lesions associated with tuberculosis of the viscera, which, while accompaniments of this disease clinically, did not exhibit necessarily the characteristic pathological anatomy of tuberculosis in other structures. Thus, for example, lupus vulgaris is a true tuberculosis of the skin, with the histological architecture associated with the disease in other parts of the body. The papulonecrotic tuberculid, on the other hand, is a localized non-specific type of inflammatory reaction, the individual lesions being papules occurring by preference upon the extremities, each distinguished by a central necrotic plug, which, on separation, permits the healing of the lesion with the formation of a punctate, atrophic scar. Upon the etiology of tuberculids a large amount of clinical and experimental work has been done. The relative degrees of association of the various types with tuberculosis have been widely studied. Lichen scrofulosorum, a grouped, follicular, papular eruption, has been clinically and experimentally demonstrated to be a tuberculid. The papulonecrotic tuberculid, another type of cutaneous lesion, is now generally accepted as of tuberculous origin, so that its use as a diagnostic criterion in the identification of tuberculous lesions, frank or occult, is justified by a large body of clinical and experimental evidence. Two types of papulo-necrotic lesions with distinguishing characteristics are given separate names in the majority of dermatologic texts. These are acnitis, the papulonecrotic tuberculid of the face, first clinically defined by Barthelemy, and folliclis, the papulonecrotic tuberculid of the extremities. Of the two, the former is stated by Jadassohn to have the more distinctively tuberculoid histopathological structure. A third type of tuberculid, one degree removed, so to speak, from final demonstration as a manifestation of tuberculosis in the skin, is the so-called erythema induratum of Bazin, a plague-like lesion prone to ulceration, most often found upon the lower extremities, especially the calf of the leg. The tuberculous character of this lesion, in spite of its inflammatory architecture, is now practically conceded, especially as a result of the recent rapid advances in methods of demonstrating the tubercle bacillus by animal inoculation, antiformin digestion, etc. It also is a lesion of marked diagnostic value in the recognition of obscure tuberculosis. A number of other lesions for various reasons are now held to be tuberculids, among which might be mentioned acne scrofulosorum, pityriasis rubra pilaris, certain exfoliative erythrodermias, acne necrotica, acne cachecticorum, lupus pernio and the sarcoids. The possible tuberculous relations of lupus erythematosus and of purpura, erythema multiforme and erythema nodosum are also subjects of recent and active discussion. The material of the Mayo Clinic seems to be exceptionally rich in tuberculids, and this has afforded a number of opportunities to study the clinical and diagnostic relations of those types now accepted as on a definitely tuberculous status—the papulonecrotic tuberculid and erythema induratum. I have, moreover, discussed 8 of the cases in the present series of 30 from the standpoint of the relation of erythema nodosum to tuberculosis.*

The crux of the discussion of tuberculids among dermatologists and immunologists has centered about their pathogenesis. This point was admirably brought out in Jadassohn's masterly review of the subject just before the War. It was also dealt with in a symposium before the meeting of the Dermatological Section of the American Medical Association (1918), the discussions to appear in the *Journal of Cutaneous Diseases* during the year. The problem of investigators has been to explain how a lesion, which in pathological architecture is not tuberculous, can present such an unvarying association with a tuberculous focus as that found in the papulonecrotic and erythema induratum types of tuberculids. The theories on which work was at first conducted followed the familiar toxic lines and ascribed the cutaneous lesions to tuberculotoxins elaborated at a distant focus. The development of experimental methods has, as already intimated, relegated this theory increasingly to the background and brought forward more and more convincing evidence that the tubercle bacillus itself, probably hematogenously distributed, is responsible for the individual lesions of a tuberculid. While organisms are exceedingly difficult to demonstrate in these tissues, positive results are claimed, and the percentage of successful animal inoculations is rising above the margin of experimental error for this mode of establishing tuberculosis. But the demonstration that the tubercle bacillus, whether in virulent or attenuated form, is responsible for the lesion is not adequate to explain why in one case hematogenously distributed bacilli gave rise to tubercles and epithelioid changes and in others to merely non-specific inflammatory reactions with necrosis or to fibroid changes of a quasi-neoplastic instead of granulomatous character. In animal experimental work it has been shown that the tubercle bacillus can persist as an embolic invader in veins without setting up more than trivial changes (Liebermeister). Through the work of Saeves in trichophytoses a similar condition of insusceptibility of tissues has been recognized in these diseases. One explanation, that of a difference in the virulence of the invading organism, has had

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* Study I, "Tuberculous" purpura, erythema multiforme and erythema nodosum.

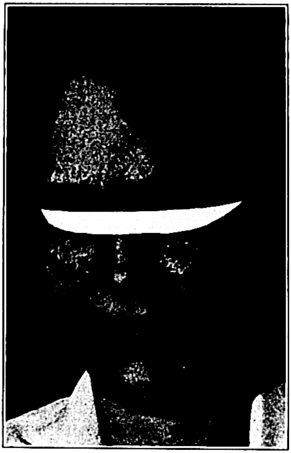

FIG. 1 (191446).—Acnitis, the papulonecrotic tuberculid of the face. Patient had had tuberculous peritonitis. Note the central necrotic plugs and the uniformity in size and age of the lesions. The crop appeared following quinsy, was treated as acne vulgaris and was ascribed by the patient to nux vomica.

numerous proponents. It has, however, gradually given place to an explanation based on the different reactivity of different persons and even of different tissues to the organism. In other words, cutaneous allergy or hypersensitiveness has been invoked to explain why one person develops lupus vulgaris, another a papulonecrotic tuberculid, another lichen scrofulosorum and still another, perhaps, a sarcoid. The importance of the allergic factor was effectively demonstrated in the experimental work of Rist and Rolland, and there can be little doubt that while its significance may be overestimated by some investigators, it is one of the best available explanations of the phenomena. For a fuller consideration of the experimental work underlying this theory, reference should be had to the studies of Gougerot, Rist and Rolland and Zieler.

Thus far the principal emphasis has been placed on tuberculin and tuberculo-toxins themselves as the agents that sensitize the tissues to the hematogenously distributed bacilli. Ingenious explanations have been devised to account for the observed failure of certain persons with tuberculids to react to tuberculin in the von Pirquet or intradermal tests. These follow the immunological conceptions applied in explaining the failure of extreme stages of tuberculosis to react to tuberculin. Thus far, however, little account has been taken of the possibility that sensitizing agents other than tuberculin may be responsible for a part of the allergy which makes a tuberculid possible, and that the person who does not react to tuberculin fails to do so because he does not owe his sensitiveness to tuberculin but to some other toxic substance or bacterial product. This point will be raised again in pointing out the association of tuberculids with pyogenic foci of infection, as evidenced in this series. The mechanism of the allergic reaction which results in the formation of the papulonecrotic tuberculid is, roughly, as follows:

Bacilli are carried by the blood stream to a hypersensitive skin and deposited at points where the circulation best favors the lodgment of an embolus—namely, in the extremities. At once a local anaphylactic reaction is set up, an inflammatory papule forms and at the point where the reaction is most intense disintegration of the tissues occurs with central necrosis. In the reaction the organisms which precipitated it are largely destroyed, which accounts for the excessive rarity of their demonstration. The pathological picture is that of an acute inflammation and is practically identical in the papule of a von Pirquet reaction, the papule of folliclis or acnitis and the lesions of erythema induratum. While a tuberculid may not be tuberculosis cutis histopathologically, it is due to the tubercle bacillus, and as such is evidence of its presence in the body. This, in effect, summarizes the trend of modern opinion. It should not be forgotten that, like all generalizations, this one has its borderline, and that it is possible to demonstrate lesions which clinically are tuberculids yet have the architecture of tuberculosis (Harris's case of dermatitis nodularis necrotica as illustrated in Pusey's *Principles and Practice of Dermatology*).

Tuberculids of the papulonecrotic and erythema induratum type, when recognized, have a considerable value to general diagnosticians as earmarks of obscure tuberculosis. An understanding of their pathological and clinical background often throws much light on elements in the patient's general condition, which may be ignored or misinterpreted. A preliminary description of the type here considered will be of assistance in a comprehension of these relations.

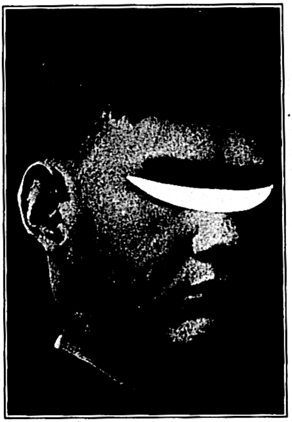

Fig. 2 (200229).—Acnitis, the papulonecrotic tuberculid of the face in a patient with tuberculous adenitis, showing the involvement of the ear by the tuberculid. The black spot in the helix is an active lesion. "Moth-eaten ear."

It must be borne constantly in mind that the distinction between types of papulonecrotic tuberculids—that is, folliclis—the papulonecrotic tuberculid of the hands, or acnitis, that of the face, is largely for clinical convenience, and that one is not exclusive of the other. All the various forms may be present at the same time in the same person or in succession at different periods of his history. The identification of the elementary lesion of a tuberculid, or in fact of any dermatosis, is the first requisite to a diagnosis. The elementary papulonecrotic lesion is exactly what its name indicates. Whether occurring on the face, the hands, the buttock, the legs, the toes, the ears, it is an inflammatory papule exhibiting, in fully developed form, a central necrotic plug of tissue, usually dark in color. In its earlier stages the papule may vesiculate, later drying enough to show the necrotic plug. The plug may, in the later stages of the lesion, either suppurate out or be picked out by the patient, leaving a conical depression which heals, producing a punctate atrophic scar. The inflammatory process which produced the papule also gives rise to a ring or collarette of hyperpigmentation about the scar, which persists for periods of months or even years in certain situations, especially on the lower extremities, where stasis accentuates the process. A papulonecrotic lesion may vary in size from a large pinhead in folliclis to a pseudofuruncular lesion several centimeters across in dermatitis nodularis necrotica, but if careful examination is made the primitive or essential lesions can usually be found.

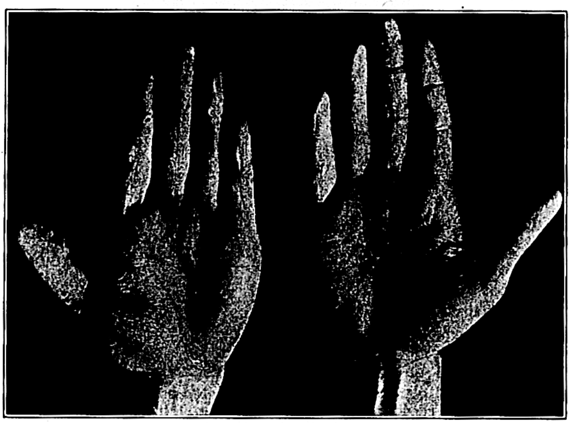

FIG. 3 (226884).—Various types of folliclis, the papulonecrotic tuberculid of the hands. An active lesion on the fourth finger of the left hand. Note the typical crater left on removal of the necrotic plug. Patient with tuberculous adenitis.

Failure to recognize papulonecrotic lesions or their scars is quite as often due to faulty methods of examination as to unfamiliarity with the lesion. The localizations and sites of predilection of the lesions are often not inspected by the internist, who is interested in percussing the chest or palpating the abdomen. Instead of making a purely objective examination of the entire body, the busy diagnostician, guided by the history, is likely to overlook the moth-eaten ear of acnitis unless he is expecting gouty tophi. In the same way the backs of the terminal phalanges and the tips of the fingers, the favorite localization for the form of papulonecrotic tuberculid known as folliclis, are seldom the subjects of painstaking inspection by general diagnosticians. Punctate atrophic scars about the elbows and the extensor surfaces of the forearms are attributed to furuncles and trauma instead of to the tuberculid responsible for them. A poor light, as well as cursory inspection, is responsible for many misconceptions of these lesions. Surprising and entirely unwarrantable operative interference may be practiced upon tuberculids of the leg through insufficient observation or faulty interpretation. Incisions for drainage, excisions with suture, skin grafts and transplants, excisions for diagnosis, with a report of "fibroma," "inflammatory tissue," etc., are frequent. The exquisite tenderness of many of the larger leg lesions combined with central softening is misinterpreted as osteomyelitis or furunculosis and subjected to operative trauma.

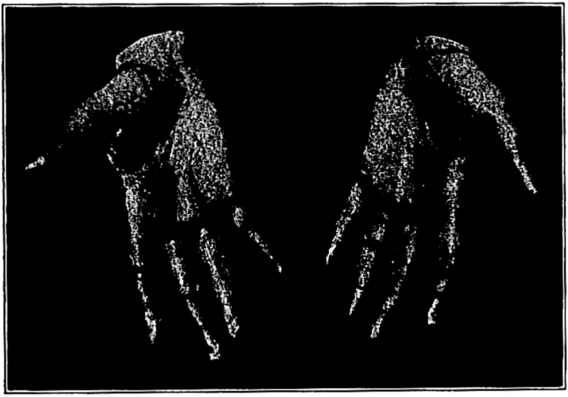

Fig. 4 (212370).—Folliclis in a patient with erythema induratum. Note the various stages—a fresh papule on the patient's right little finger, vesicle formation and beginning necrosis on the left little finger, active lesions with central necrosis on the right index and middle finger, scars on the left index and middle fingers.

Erythema induratum is in a sense only an exaggeration of the papulonecrotic lesion. In fact, the larger lesions often seem to be produced by a confluence of smaller nodes. The typical lesion is an erythematous to violaceous plaque usually several centimeters in diameter, firm, indurated and somewhat tender. By predilection these lesions are said to appear on the posterior aspect of the leg in the region of the calf and ankle, but this localization in my experience is by no means constant. Lesions varying all the way from the small necrotic centered papule, through the breaking down nodule to the typical ulcerating plaque may be found scattered about the lower, and at times even the upper, extremities. In fact, the presence of papulonecrotic lesions is a material aid in diagnosis of a solitary ulcerative plaque of erythema induratum.

The scars of tuberculids are in many ways quite distinctive. This is especially true if their distribution is limited to one or the other of the sites of predilection. A number of these sites with their characteristic lesions and scars are illustrated in Figs. 1–8, 11, 12, 14, 15, 18 and 20. The scar is never contractile or distorting, and in the peculiar punctate atrophy produced may suggest that of a variola, though it is usually deeper.

SUMMARY OF DIFFERENTIAL DIAGNOSIS.

Papulonecrotic Tuberculid of the Face—Acnitis. This condition is to be distinguished from acne vulgaris by the circumscribed papule with central necrosis as distinguished from a pustule or infected comedo and by the uniformity of the lesions, which tend to appear in crops and hence to be, to a considerable extent, of the same age and size. The moth-eaten ear, due to papulonecrotic lesions in this site, is illustrated in Fig. 2. The absence of comedones and seborrhea and of transition lesions from comedone to pustule is significant. Acute acnitis may strongly suggest variola from which its course distinguishes it.

Papulonecrotic Tuberculid of the Extremities—Folliclis. When limited to the hands and feet, there is practically no other lesion which closely simulates it. In the vesicular stage the marked inflammatory papule which forms the bulk of the individual lesion, and the tendency to become hemorrhagic distinguishes it from the sago-grain vesicle of dysidrosis, pompholyx or "sweat eczema," which moreover does not leave scars. In the case of folliclis the patient describes a highly characteristic sign—a feeling as if a thorn were pressing into the flesh when the papule is pressed upon. Their small size and uniform appearance and a frequent tendency to localize in faceted patches or on the dorsal surface of the phalanges, help to distinguish the scars from those of trauma. In cases with marked vasomotor disturbance the diagnosis of Raynaud's disease may be made through failure to observe the scars or to get a careful history of the course of the lesion. Frost-bite is a more diffuse erythematous lesion. Lupus pernio may temporarily simulate folliclis, but the distinction can be made by a search for the elementary lesion and its evolutionary steps as outlined above. The papulonecrotic tuberculid of the trunk is frequently mistaken for furunculosis and for severe acne vulgaris. Here again the search for the elementary lesion reveals it not as a comedone on a seborrheic base but as a papule in which vesicle formation may occur but is usually abortive and in which pustulation is usually secondary to the formation of the dry, hard, necrotic central plug. The large nodules undergo actual ulceration and heal slowly, suggesting ecthyma and in the pustular phase, a pustular lues. (The absence of transition stages from comedone to pustule eliminates acne.) On the arms and trunk scratch papules must be distinguished. The scratch papule is a secondary infection of a previously produced excoriation, and uninfected or recent excoriations, dried bloodstreaks, linear abrasions and scars can usually be found. Parasites produce the picture of a scratch dermatitis. The nodular lesions of prurigo and lichen urticatus can be distinguished by the fact that they have no central necroses though they show scratch excoriation. They are also accompanied by other evidences of dermatitis, or by wheals and multiform erythematous lesions. The pruritic nodules of Hodgkin's disease may suggest a tuberculid, but their intensely pruritic character and the multiple evidences of scratching, including the history of violent itching, together with the absence of central necroses, eliminate the tuberculid. The nodules of Hodgkin's disease do not primarily localize on the extremities. I have known a generalized tuberculid to be diagnosed a psoriasis in the presence of marked crusting, the diagnostician forgetting that psoriasis does not produce scars.

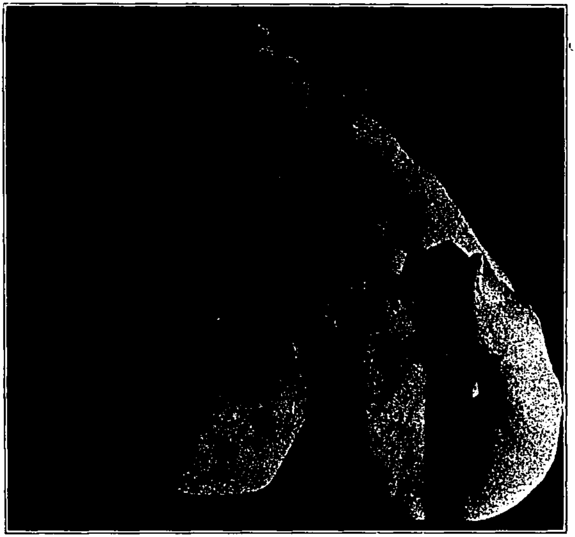

FIG. 5 (228772).—Folliclis localizing at points of greatest trauma. Patient with tuberculous glands.

Papulonecrotic Tuberculids of General Distribution. These lesions may occur in showers, especially involving the trunk. Their tendency to show a vesicular stage and the necrosis as distinguished from pustulation helps to eliminate a pustular syphilide. The diagnosis of this type of lesion may offer great difficulties, and not infrequently the conclusion must depend upon collateral evidence of the presence of tuberculosis and the absence of syphilis and upon recurrence and chronicity. One such case in my series yielded a positive Wassermann reaction on several occasions, and only the recurrence of the lesions through a period of years and the final occurrence of typical necrotic papules made the differentiation possible. The scars of a widely distributed tuberculid may suggest those of a pustular syphilid so strongly that serious mistakes may be made. In one such case a positive Wassermann and a mass of glands which cleared under arsphenamin seemed to establish a diagnosis which was reversed by later findings.

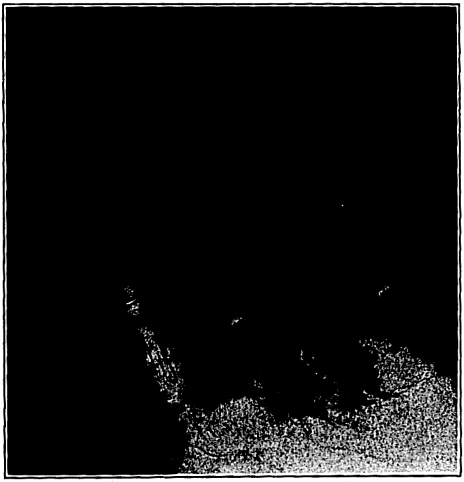

FIG. 6 (230740).—Facetted, grouped scars of folliclis, index, middle (tip) and fourth fingers. Vasomotor abnormalities, tuberculous adenitis.

There is a distinct tendency for papulonecrotic tuberculids to occur at points of trauma. This fact has, in my experience, led to confusion with epidermolysis bullosa hereditaria, especially when lesions were localized on the elbows. One distinctive site of lesions in epidermolysis bullosa hereditaria, over the thyroid cartilage of the larynx from collar trauma, I have never known to be the site of tuberculids not involving the face. Moreover, the bullous phase of epidermolysis is much more marked than the vesicular phase of tuberculids, which is often abortive. Nevertheless, the scarring produced by the two conditions may have many points of similarity (Fig. 6).

Erythema Induratum. This condition seldom occurs alone. It usually is associated with papulonecrotic lesions that may group to form larger plaques. The differentiation from nodular lues depends first upon the tendency of the lesions to symmetrical distribution on both extremities, and second, upon the multiplicity of the lesions and their lack of configuration, that is, their irregular shape and arrangement as distinguished from the grouping into typical arciform or polycyclic arrangements observed in lues. The scars exhibit the same peculiarities (Fig. 7). From gumma of the pretibial region, the solitary character of the gumma and the preference of erythema induratum for the posterior surface distinguish it. It should be remembered, however, that gummas may also be symmetrical and multiple. Multiple infarctions in the skin or anemic ulcers are usually only associated with high degrees of thrombotic occlusion of the vein, which can be seen and palpated

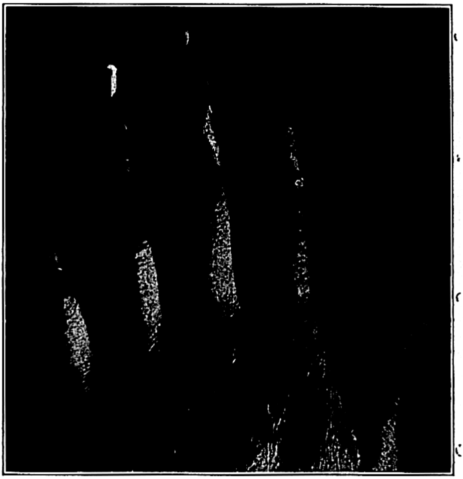

FIG. 7 (186129).—Scars of folliclis, dorsal surface of fingers. Two involuting lesions on index and middle fingers. Positive Wassermann but no clinical evidence of syphilis.

and with suggilation and hemorrhage into the skin and even multiple areas of gangrene. Erythema nodosum is usually distinguished from erythema induratum by the tendency of the latter to ulcerate, and to occur by preference on the posterior surface. As a matter of fact, all stages in the transition from erythema nodosum to erythema induratum both as regards morphology and localization, may be seen in subjects with a tuberculous background, so that some of the distinctions are artificial. Streptococcal or diphtheroid erythema nodosum of the Rosenow type, however, does not ulcerate and the process is, in general, more acute, the nodes more brawny and edematous, and the hemorrhagic and ecchymotic changes and edema more marked than in the tuberculous type. A resumé of this aspect of the problem may be found in the discussion of tuberculous erythema nodosum in the first study of this series.

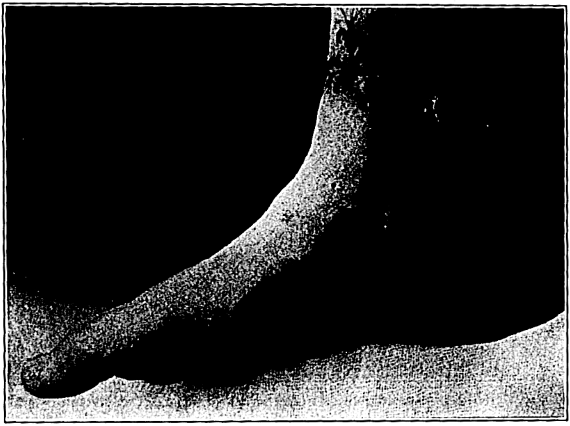

Fig. 8 (171947).—Papulonecrotic lesions on the foot and ankle of a patient who also had erythema induratum. Note the nodules that have not yet undergone central necrosis, as well as the necrotic lesions with black central plugs.

Ulcerative erythema induratum is to be differentiated from noduloulcerative syphilids again by its tendency to symmetry, which, however, is no more invariable than is asymmetry in lues. The luetic ulcer has a configuration which can be recognized by practice as segmental or arciform. The erythema induratum ulcer is irregular and nondescript. Instead of a sharp margin closely bordered by normal skin, the erythema induratum ulcer is usually undermined, has a thin grumous or hemorrhagic discharge, and is surrounded by bluish scrofulodermatous sodden tissue. There is usually no definite gummatous slough as in lues. The concomitant occurrence of papulonecrotic lesions and nodules greatly assists in the recognition of erythema induratum. The typical chronic varicose ulcer is easily differentiated by its rigid scar tissue border, its flat open floor of anemic granulations and the usual regularity of its margin. Epithelioma is usually unilateral and has a highly characteristic nodular and rolled pearly margin.

A word of warning should be given as to the use of arsphenamin in an attempt to make a differentiation between a tuberculid and a syphilitic lesion by therapeutic test. Tuberculids, as will be seen in a subsequent paper, respond rapidly to this form of medication, so that a false therapeutic effect is produced which may subject the patient to prolonged treatment for a non-existent lues.

CLINICAL RESUMÉ OF THIRTY CASES OF PAPULONECROTIC TUBERCULID AND ERYTHEMA INDURATUM.

The series of cases collected by the writer during the past two years illustrates in a convincing way the association of these conditions with tuberculosis. Of the thirty cases 80 per cent. were women. This preponderance of women over men has been recognized by others. In a series of 100 cases of tuberculous adenitis reviewed in connection with this study a similar proportion of 64 per cent. women and 36 per cent. men was observed. The youngest patient was ten years of age, the oldest fifty-one. Of 13 cases in which data were available the onset of the tuberculid had been in the second or third decade of life in 12, corresponding in this particular to the period of greatest incidence of signs of systemic tuberculosis.

Eighty-three per cent. of the 30 patients bore evidence of past or present lesions of the papulonecrotic type. Three had lesions on the face (acnitis), 12 had lesions or scars on the hands (folliclis), 15 had papulonecrotic lesions on the legs and 9 had them on the trunk. Only 2 patients presented an erythema induratum uncomplicated by another tuberculid. One of these had apparently a tuberculosis verrucosa cutis and the other had undoubted tuberculous adenitis. It is apparent that in its association with other more definitely proved tuberculids in this series, erythema induratum establishes, still further, its claim to a tuberculous origin.

RELATION OF THE CUTANEOUS LESIONS TO SYSTEMIC TUBERCULOSIS.

History of Tuberculosis in the Family or Patient. A definite history of tuberculosis in the family, sufficiently direct to bring the patient into contact with it, was given by one-fourth of the cases (23 per cent.). Somewhat more than one-third of the patients had been diagnosed as tuberculous previous to their examination in the clinic. The diagnosis was usually based upon adenopathy rather than on pulmonary or other signs.

The Objective Manifestations of Tuberculosis. It is to be understood that tuberculids as signs of tuberculosis are excluded. Fifty-seven per cent., or more than half of the entire series, showed incontrovertible systemic objective signs of tuberculosis, usually in such numbers that had any one sign been insufficient the others would have confirmed the diagnosis.

Thirteen per cent. of the cases were rated as disputable, and 30 per cent. presented no definite signs. Table I, summarizing the disputable and occult cases, is here appended.

TABLE I.

DOUBTFUL CASES.

Case A202732—Erythema nodosum; loss of weight; doubtful lung lesion as revealed by *x*-ray and physical examination.

Case A212370—Tenosynovitis, tuberculous(?) (folliclis, erythema induratum).

Case A188556—Erythema nodosum and erythema multiforme. Enlarged right cervical glands; temperature and lung signs.

Case A224920—Family riddled by tuberculosis; patient underweight; asthenic; well-defined signs in right apex (folliclis, fingers and toes).

OCCULT CASES.

Case A39183— Obscure anemia; inflammatory changes in abdomen; positive and negative Wassermann at various times, menorrhagia; headaches; generalized papulonecrotic tuberculid.

Case A197825—Florid, obese girl; no signs of tuberculosis; erythema induratum.

Case A221958—Positive Wassermann without history or evidence of syphilis; lupus erythematosus of the face; folliclis, scars on fingers.

Case A218528—Anemia, persistent; marked loss of weight; erythema induratum and papulonecrotic tuberculid of the legs.

Case A201284—Anemia, pernicious (?); extreme hyperpigmentation; cachexia; tuberculid of the legs; lupus erythematosus; adrenal tuberculosis(?).

Case A171947—General examination negative; obese, well nourished woman; extensive papulonecrotic tuberculid of the legs with erythema induratum.

Case A63167—Iritis in childhood; tuberculosis of the knee (?); three weak positive Wassermanns, without evidence of lues; alveolar abscess, otherwise negative; papulonecrotic tuberculid of legs and elbows; erythema induratum.

Case A186129—Repeated positive Wassermann; exposure, but no evidence of lues; folliclis of hands; scars of papulonecrotic tuberculid of the body.

Case A233765—Obese girl, no signs of tuberculosis, but von Pirquet strongly positive; erythema nodosum and induratum; legs and arms involved, with purpuric lesions.

The occult cases form a group of special interest. The mere fact that a gross focus of tuberculosis cannot be demonstrated is of course not an evidence that such a focus may not exist, in the retroperitoneal glands, for example, or in the uterine adnexa.[6]

Two of our patients gave histories suggestive of such a focus but in the absence of operative exploration the focus could not be demonstrated. Four of the 9 occult cases were in florid, rather obese persons, of a type recognized as predisposed to some extent to tuberculous infection.

One-third of 27 cases in which radiograms of the thorax were made showed evidence of pulmonary tuberculosis. The involvements were largely apical, with calcification and signs of healing in several. The importance of a tuberculid as a diagnostic lead for the internist can be appreciated from such a finding. Four cases showed doubtful *x*-ray signs of little independent value. One-third of the cases likewise presented physical signs suggestive of pulmonary tuberculosis. Both physical and *x*-ray findings were present in 5 (17 per cent.) of 29 cases.

More than two-thirds of the patients had a visible and palpable lymph-adenitis, making glandular involvement the commonest form of tuberculosis associated with these tuberculids. In 38 per cent. the adenitis was marked. This very evident association of tuberculids with glandular tuberculosis forms a theoretical basis for explaining their presence in occult cases without visible manifestations. Moreover, the association of tuberculids with a form of tuberculosis that, in a broad way, indicates a high individual resistance to the bacillus is of interesting prognostic significance, and suggests that a tuberculid, among other signs, may be in a way accepted as evidence of a benign course of the disease. This point is of interest in connection with the older conceptions of the extreme gravity of the papulonecrotic tuberculid in infancy. A recent study by Hempelmann has brought forward evidence to show that even in infancy the association with lymphatic tuberculosis (tracheobronchial node involvement) can be recognized, and that the prognosis in cases with tuberculids is no graver than in those without.

Among other forms of tuberculosis with which tuberculids in this group were associated the following should be mentioned: sacro-iliac abscess, tuberculous peritonitis, renal tuberculosis (bacilli demonstrated) and tuberculosis verrucosa cutis one case each, tuberculous keratitis 3 cases. In one patient the tuberculosis verrucosa cutis occurred on the right leg, the erythema induratum on the calf of the left.

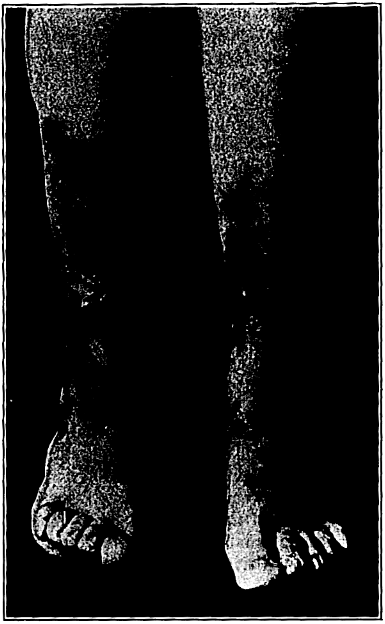

FIG. 9 (171947).—Serpiginous ulcers produced by the confluence of solitary nodules and plaques. Scar of unwarranted surgical interference on the left leg.

Prevalence of Tuberculids in Connection with Tuberculous Glands. In endeavoring to ascertain the prevalence of tuberculids in cases of tuberculous adenitis, as observed by internists in the material of a large clinic, 100 cases of tuberculous adenitis were reviewed for evidence that any cutaneous lesion had been observed. In this series 10 per cent. were described as having lesions which could be inferred to be tuberculids. The proportion of men to women among those having cutaneous lesions was as 1 to 10, which is not far removed from the percentage observed in the series of tuberculids under discussion. There can be little doubt that a number of the less obvious tuberculids were overlooked and that 10 per cent is too small a figure for the incidence of these lesions in glandular tuberculosis.

A careful comparative study of the cutaneous lesions and the types of tuberculous systemic involvement failed to reveal any constant relation between the tuberculous focus and the type of tuberculid. On the other hand, a definite relation between vasomotor and stasis phenomena and the distribution of the tuberculid, was apparent. There was also evidence to show that the more extensive tuberculids in a rough way were associated with what seemed the more extensive and serious types of systemic tuberculous involvement. Seven of the 9 cases presenting extensive tuberculids involving trunk and extremities also presented the most serious forms of tuberculous involvement in the series.

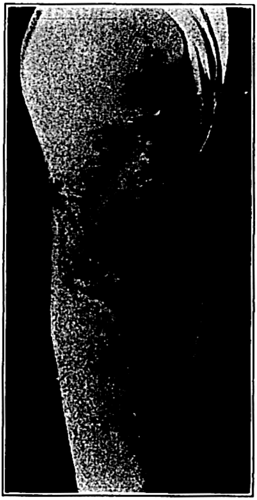

FIG. 10 (219380).—Solitary gummatous ulcer with edema and infiltration of the surrounding tissue, to show the differential points.

RELATION OF VASOMOTOR PHENOMENA AND VASCULAR STASIS TO THE DISTRIBUTION OF TUBERCULIDS.

It has long been recognized that a tuberculid tends to appear upon the extremities, and especially to appear in those patients in whom the peripheral circulation is feeble or obstructed. Data on the collateral local vascular findings were collected on 28 cases in this series. Of these one-half (50 per cent.) showed abnormalities of the vascular supply in the form of cyanosis and vasomotor anomalies of the extremities, and swollen hands, legs or feet. Every "stasis leg," that is one with a tendency to passive congestion from defective venous return, had erythema induratum. Five of 7 with blue hands had folliclis. The possession of a leg with a tendency to vascular stasis thus predisposes, to the extent of nearly 100 per cent., to the type of tuberculid known as erythema induratum.

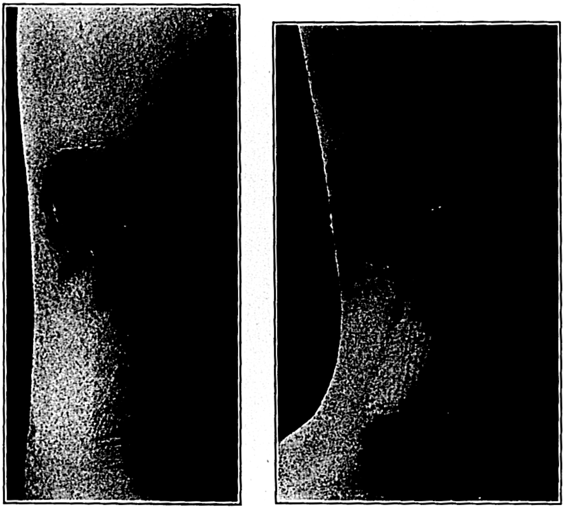

FIG. 11 FIG. 11*a*

FIG. 11 and 11*a* (218528).—**Erythema induratum with papulonecrotic lesions on the legs of a patient of the "occult" type.**

In the same way, the possession of cold, clammy, mottled hands predisposes to the extent of more than 70 per cent., to the development of folliclis. It was a matter of note that all the patients who, at the onset of their cutaneous lesions, had been overweight showed the severest part of their manifestations in the lower extremities; a fact which accords well with the vascular stasis usually present in such legs. Obese persons, therefore, seem to be predisposed to the erythema induratum type of tuberculid, and the thin and neurotic with marked vasomotor imbalance, to folliclis. Only 2 of 7 obese patients had folliclis, and one of these was a child with a

Summarizing the series as a whole from the standpoint of localization of lesions, more than half (57 per cent.) of the patients had lesions on the upper extremities, but almost three-fourths (74 per cent.) had them on the lower extremities, showing the distinct predilection for parts of slower circulation. Ninety-six per cent. of the patients, or practically all, had lesions on either upper or lower extremities. Twenty-three per cent. had lesions on the upper extremities and not on the lower; 43 per cent. on the lower and not on the upper, so that the odds are 2 to 1 in favor of the lower extremity as a site of involvement. One-third had involvement of both extremities, one-third showed involvement of the trunk, and one-fifth of the face. It is of interest to note that 65 per cent. of those in whom the face was involved had lesions on the ears, and that the ear was the seat of lesions in 13 per cent. of the whole series (Fig. 2).

The importance of the circulatory factor in the distribution of tuberculids is one of the strongest arguments for the bacillemic as opposed to the toxemic origin of the process. The presumption is that at points where the circulatory stream is moving most slowly the maximum opportunity for the deposit of organisms will present itself, and that lesions will tend to appear, as they do, in areas where one factor or another acts to delay the movement of the blood.

MISCELLANEOUS FINDINGS ON EXAMINATION.

In the study of this series of cases a number of interesting miscellaneous findings developed. The recognition of concomitant tuberculosis in cases exhibiting a tuberculid is, on the whole, a matter of identifying signs by objective examination rather than of eliciting symptoms. Six of the patients had a temperature of 99° or over at the time of examination, although temperature is a much more important factor at onset, especially in those cases which begin as erythema multiforme or erythema nodosum. Of a series of 7 such acute cases, 5 showed temperatures varying from 99° to 103°. Cough had been a well-defined symptom in only 7 of 25 cases, or less than one-third; night-sweats occurred in none, sputum in only 2, both negative for bacilli. On the other hand, amenorrhea was a definite symptom in 43 per cent. of the cases, and in some was coincident with the greatest activity of the tuberculid. Losses of weight, varying from 2 to 45 pounds occurred in 40 per cent., more than half losing less than 10 pounds.

The periodicity of tuberculids and their tendency to exacerbation in spring and fall, which is an important factor in treatment and an aid to diagnosis, were apparent in nearly half of 20 cases in which data were obtained. More than three times as many recurred in spring as in fall, and one-fourth of the patients had lesions continuously.

A little less than half the cases presented secondary anemias with a hemoglobin below 70 per cent. (Dare). In one-fourth of the cases it was below 53 per cent., the lowest being 30 per cent. In the latter case a possibility of a pernicious anemia was entertained. From two of the anemias the influence of syphilis could not be eliminated. Accompanying the anemia was a tendency to leukopenia. Even in the acute cases the patients did not, while febrile, exhibit any tendency to leukocytosis. Thirteen of 25 patients had counts below 6600, 8 below 5800. Only 3 exceeded 10,000. No differential counts were taken. On the score of blood-pressure 35 per cent. were below 120, the lowest 98; 40 per cent. were normal,

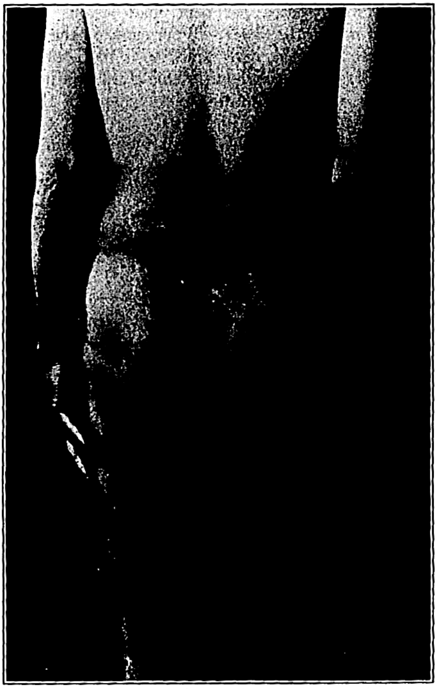

FIG. 12 (226884).—Scars and pigmented residue of acne scrofulosorum, the papulonecrotic tuberculid of the trunk in a patient with tuberculous adenitis. Note lesions on the extensor surfaces of the forearms also. This patient also had lesions of folliclis on the fingers.

and 25 per cent. exceeded 135 systolic, the highest being 142. The higher pressures were all in persons under 31. The diastolic and pulse-pressures exhibited no distinctive variations. Observations on the Wassermann test in the tuberculids will be included in the discussion of allergic manifestations.

It is apparent from this review that the clinical accompaniments of a tuberculid tend to be those of a low-grade tuberculous infection. A moderate secondary anemia and leukopenia with occasionally an afternoon temperature, most likely to appear during exacerbations; moderate loss in weight; occasionally cough associated with a lighting up of the acute process, and signs of a definite but not fulminating process in the lungs or glands make up the average clinical picture in a large percentage of the cases. The florid type of case must constantly be borne in mind in dealing with tuberculids, and mere robustness, weight and color must not be accepted as invalidating a diagnosis based on the tuberculid.

THE TUBERCULID IN DIAGNOSIS.

While some caution must be exercised in inferring the diagnostic career of a case from the patient's history or examination, such a study of our series of cases suggested several points of interest. In only 5 of the 30 cases referred for diagnosis to our department had a correct diagnosis been made, and tuberculosis on the score of their cutaneous manifestations had not been suspected. In 2 of the 5 cases the diagnosis might have been made by the internist, but was later made by a dermatologist before the patient was seen by us. In more than one-third of the cases the tuberculid had either been overlooked or ignored as insignificant. This was especially true of acnitis on the face and of folliclis on the fingers. In another third of the cases the cutaneous lesion had been misdiagnosed, to judge from the history or treatment. Six of the 9 cases in this second group had been interpreted as syphilitic, 3 because of the finding of a positive Wassermann, a point to be discussed in connection with allergy. Two were interpreted as luetic because of the history of what was probably a general or extensive shower of tuberculid lesions, of which the scars were present. Another point which seemed to suggest lues was the history of arthritis, myalgia and indefinite pains with mild anemia often given by these patients. Six cases, or one-fifth of the series, had sustained probably needless operative procedures in the effort to make a pathologic diagnosis from the lesions, or for excision, curettage or drainage. The vasomotor and stasis factors had led to a diagnosis of Raynaud's disease in one case, and varicose ulcer in another. One, because of lesions on the elbows, in spite of obvious scars, sustained a diagnosis of psoriasis.

It is apparent that unfamiliarity with the lesions and failure to observe, whether due to poor light or other cause, together with the tendency to interpret a tuberculid as syphilis, account for four-fifths of the diagnostic errors. For the former difficulty the remedy is obvious. For the latter it should be recalled that not all skin lesions that occur in the presence of a positive Wassermann reaction are syphilitic, and that the recognition of syphilis does not remove the obligation to ferret out an associated tuberculosis, particularly when the cutaneous evidence points toward it. The occurrence of false positive Wassermann reactions from cholesterinized antigens in the presence of tuberculosis and the absence of syphilis is also being gradually established. The occurrence of tuberculids in crops, their wide distribution upon the face, trunk and extremities, and the frequently associated myalgias and arthralgias are the points in the

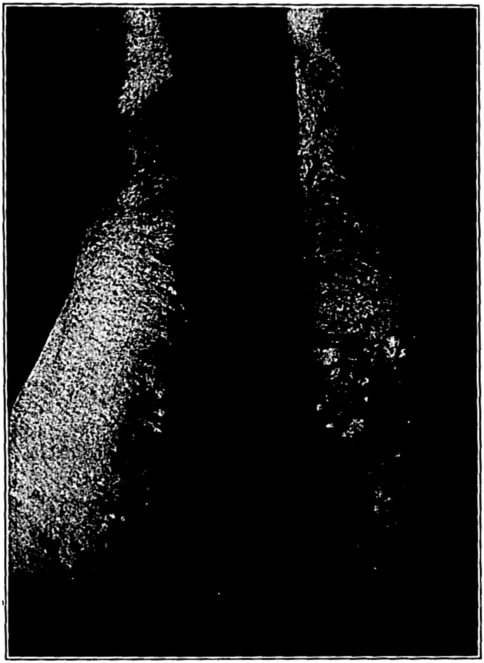

FIG. 13 (234128).—Characteristic scarring and active lesions of the papulonecrotic tuberculid on the elbows of a patient with tuberculous adenitis.

history which seem to suggest lues and septic foci rather than obscure tuberculosis to the casual mind. The usefulness of the tuberculid in determining the character of an adenopathy was attested in several cases in which internists had estimated the diagnostic possibilities of cases at 30 to 70 per cent. in favor of Hodgkin's disease, and asked for excisions for diagnosis before seeing the report of the dermatologist.

THE COLLATERAL INFECTION FACTOR: ANAMNESIS.

One of the most interesting relations brought out by this clinical study of the tuberculids was that of collateral types of infection shown in the history and in the examination. In the histories of these patients, five syndromes stand out with overwhelming prominence. These are tonsillitis and "rheumatism;" and pneumonia, grippe and pleurisy. The extraordinary prevalence of these two types of infections, representing the focal infections traceable to tonsillar and alveolar pathology and the respiratory group may be seen in Table II. Since the records in these cases were taken by men who had no conception of a possible relationship between the dermatosis and the systemic condition, they are probably quite unprejudiced.

TABLE II.

HISTORY OF ACUTE INFECTIONS.

Case.	Tonsillitis.	Rheumatism.	Pneumonia.	Grippe.	Pleurisy.
200229	X	..	..	X	
202732	..	..	..	X	
186129	X	X			
200833	X	..	X	X	X
212370	X	X			
194150	X	X	X	X	
157847	..	..	..	X	
169350	X	X	..	X	X
174923	..	X	X		
39183	..	..	X		
188556	..	..	..	X	
197425	..	X	X	X	
221958	..	..	..	X	
154673	..	..	..	X	
228021	X				
49238	..	X			
224920	X				
228772	X	..	..	X	X
218528	..	..	..	X	X
161592	X	..	X		
191446	X	X			
201284	..	..	..	X	
171947	..	..	..	X	
63167	..	X	X	..	X
230740	..	X			
226884	..	X	X		
233765	..	X	..	X	
234128	..	X			
Total	11	13	8	15	5
	39%	46%	29%	54%	18%

Summarizing Table II, it appears that of 28 patients, 39 per cent. had had tonsillitis and 46 per cent. had had rheumatism. Twenty-nine per cent. had had pneumonia, 54 per cent. had had grippe, and 18 per cent. had had pleurisy. Nearly 70 per cent. had had tonsillar infections or rheumatism; 62 per cent. had had definite respiratory infections, not including pleurisy.

TABLE III.

APPARENT ETIOLOGIC CONNECTIONS.

Case 186129—Outbreak of general papulonecrotic tuberculid in the spring following a winter of repeated tonsillitis and colds.

Case 169350—Five years of rheumatoid pains. Grippe followed by pleurisy and abdominal symptoms two years previous to examination; loss of weight, then outbreak of a papulonecrotic tuberculid. No improvement from tonsillectomy.

Case 154673—Grippe; while recovering, purpura and a papulonecrotic tuberculid.

Case 188556—"Cold," with temperature, erythema nodosum, marked glandular enlargement on the right side of the neck, signs over right apex.

Case 197425—Pneumonia 1914, "rheumatism" 1914–1917, then grippe and an outbreak of erythema induratum.

Case 212370—Tonsillitis, followed by tuberculid, rheumatism, hydrarthyrosis, tenosynovitis, tonsils removed without benefit, appendectomy no effect, cleared under treatment for the tuberculid. Teeth negative.

Case 191446—Folliclis for many years following tuberculous peritonitis. Quinsy three months previous to examination followed by an abrupt outbreak of acnitis in addition to the folliclis. Alveolar abscess.

Case 230740—Pneumonia 1913, axillary glands then enlarged, removed in 1916, coincidentally with onset of tuberculid.

Case 174925—Pneumonia sixteen years previously, followed by enlarging glands, removed by operation nine years later. Removal of the glands was followed by severe rheumatism, continuous up to present time. Tuberculid appeared one year after operation; glands recurred.

By the term "rheumatic symptoms" in the foregoing discussion is meant the group of myalgias, neuritides, arthralgias, and occasional arthropathies which do not fall definitely into the category of acute articular infections. So striking has been the association of this nondescript group of symptoms with the tuberculids that it is now our practice in addition to the routine search for a focus of pyogenic infection in tonsils or teeth, to ray the chests of patients who, in association with suspicious eruptions, complain of "rheumatism."

THE COLLATERAL INFECTION FACTOR: FINDINGS.

Examination of the Tonsils. Data on the clinical condition of the tonsils were available in 21 cases of the 30. It is to be regretted that no pathologic examinations were made in those patients who sustained tonsillectomy while they were under observation. The information derived from clinical examination by an otolaryngologist was briefly as follows:

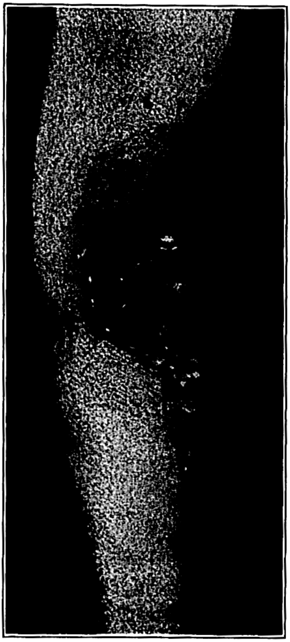

FIG. 14 (228772).—Tuberculid scarring on the elbows.

An exceptional degree of tonsillar infection seemed to prevail in the series as a whole. One-half of the patients were rated as having large and badly infected tonsils. The other half were passable and borderline cases. Practically none were entirely within the limits of normality. On the other hand, curious contradictions seemed to exist in the picture. Almost an inverse ratio appeared to prevail between the condition of the tonsil and the severity of the tuberculid. Certainly there was nothing to indicate that the severe tuberculids were directly associated with severe tonsillar infection as seen in purely clinical examination. To confirm this evidence of the absence of direct causal relation between tonsil and tuberculid it appeared moreover, that:

FIG. 15 (103534).—Scarring about the elbow of a patient with epidermolysis bullosa hereditaria.

1. The tonsils in patients with tuberculous signs were no worse than in those without. They should have been worse in the latter if they were to play the sole etiologic role.
2. No one tuberculid seemed to bear any special relation to the condition of the tonsils.
3. The tuberculid appeared after tonsillectomy in 3 instances.
4. Tonsillectomy performed in 7 instances failed to prevent or modify the course of the tuberculid.

In the light of these considerations it would appear that there is an indirect relation between infected tonsils and the presence of tuberculids, but no direct relation, both in the history and examination. In other words, the septic tonsil is probably not the tuberculous focus. If it is a factor in the situation, its more probable role is that of a predisposing or contributing factor.

Examination of the Teeth. This very important examination was not begun as a routine, unfortunately, until comparatively late in the series, when in studying the clinical picture, the frequent occurrence of a secondary focus became apparent. The results of an examination of 9 cases by x-ray showed alveolar abscesses in 3 and a rarefying osteitis of the alveolar process in one. The presence of definite dental pathology in 45 per cent. of the few patients examined is highly suggestive. It should be emphasized that gross examination of the teeth may afford no clue to the condition beyond the suspicions aroused by dental work which is founded on devitalized teeth. That the alveolar focus is not the leading factor in the production of a tuberculid is again evidenced by the fact that it is not invariably present, and that in two cases in which the teeth were normal to examination and tonsils were out (in one of the two even the appendix was removed) the tuberculid and the accompanying arthritic manifestations, including a tenosynovitis, remained unaltered until the institutions of measures directed against the actual or presumptive tuberculous focus.

It should not be forgotten that the search for a secondary focus in connection with a tuberculid should not terminate with tonsils or teeth. In one of our cases the history and findings suggested an infected gall-bladder as a focus, although the teeth were negative and the tonsils were only moderately involved.

THE POSSIBLE BEARING OF CERTAIN ALLERGIC PHENOMENA ON THE ETIOLOGY OF TUBERCULIDS.

Reference was made in the earlier part of this paper to the growth of a body of clinical and experimental evidence in support of an allergic factor in the etiology of tuberculids. As the prime exciter of the cutaneous allergy theoretically necessary to produce the non-specific types of reaction represented by tuberculids, tuberculotoxins have been accepted by investigators apparently with wholehearted enthusiasm. Undoubtedly their role is an important if not the major one. This enthusiasm has for the time being excluded from the field of vision other agents besides tuberculotoxins which are able to excite a non-specific type of cutaneous allergy. For some years the cutaneous allergy of late syphilis (Umstimmung), for example, was regarded as highly specific, and the enthusiasm with which luetin was received and used was evidence of this uncritical point of view. It was not until certain observers somewhat more skeptically inclined than the average, such as Boas, began to note the behavior of the skin to controls for luetin, that a field was opened for a non-specific interpretation. Sherrick's observation that the allergy of late lues, as evidenced by reactivity to luetin could be artificially produced by the administration of potassium iodide was a major contribution. In 1916 I argued upon theoretical grounds that the behavior of luetin was not due to the spirochetes which it contained but to an adsorption complex in which agar, the culture medium, probably played a principal role. Acting on the theoretical considerations then presented, I succeeded in showing that agar in proper concentration makes an entirely satisfactory substitute for luetin in the luetin test as applied to late syphilis, and that accordingly the reaction and the allergy on which it depended were alike non-specific. In the course of my study of this phenomenon I was able to demonstrate that an allergy clinically similar to the non-specific allergy of syphilis could be artificially produced by the intradermal injection and lysis of even an autogenous and homologous protein. In this experimental work I employed an emulsion of normal skin, both my own and that of my assistant. As a result apparently of a series of injections of this allergy-producing protein, my assistant and I developed a reactivity to agar which in all respects imitated the allergy of late syphilis. This is essentially an experimental proof of the fact that cutaneous allergy of some types as observed in a disease such as syphilis can be artificially imitated by the intradermal introduction of other proteins than those of the specific organism of the disease. While it is not offered as adequate explanation of the allergic phenomena in tuberculosis as manifested in the development of tuberculids, it is at least suggestive of the idea that proteins other than tuberculo-toxins may be responsible for the allergy that makes tuberculids possible. Such proteins may, in the light of the foregoing clinical observations, be staphylotoxins and streptotoxins, derived from what I have called the secondary focus observed in these cases. It is not impossible that the lysis of such toxins in the body or even of the bacteria themselves in recurrent bacteremias may so sensitize the skin that an embolus of tubercle bacilli will provoke a violent inflammatory reaction of a wholly non-specific character, precisely as agar does in the hypersensitive skin of late syphilis. The allergic specificity of the tuberculin reaction has not as yet been subjected to critical analysis in the light of investigations of the type detailed above. There are indications that there is a non-specific as well as a specific element in the behavior of tuberculin, not the least of which is Meirowsky's observation, confirmed by Zieler, that the sites of "syphilin" reactions react locally to tuberculin.[7]

The resemblances between the immunologic and allergic phenomena in syphilis and tuberculosis are strengthened by what is still inconclusive but highly suggestive evidence of the lapse in specificity of the Wassermann reaction when tuberculids or tuberculous allergic phenomena are concerned. The present clinical study and other observations on the behavior of the Wassermann reaction in glandular and occult tuberculosis are gradually accumulating a series of cases in which the presumption against syphilis is so strong that even a positive Wassermann must be guardedly accepted. In this series there were four cases in which positive Wassermanns had been obtained, not once but repeatedly. One of the four patients had three weak positive reactions, on the strength of which she had had intermittent treatment for syphilis for a number of years. In three of the cases treatment seemed to secure a reversal

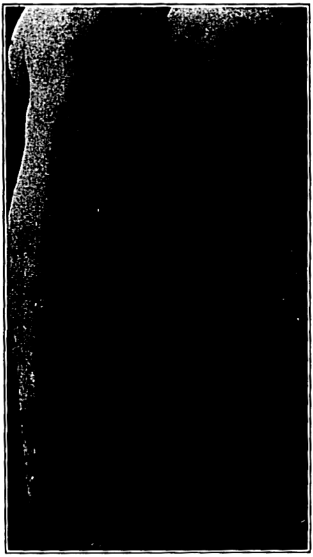

Fig. 16 (103534).—Types of scarring on the lower extremities. Epidermolysis bullosa hereditaria—the same patient whose elbows appear in Fig. 15.

to negative. On the other hand, in three of the cases absolutely no presumptive evidence of an infection has been obtained. Even the therapeutic effects observed are explainable on other grounds. In this connection I recall several cases of tuberculous glands with positive Wassermann reactions, and a case of tuberculous keratitis without evidence of syphilis which cleared up under salvarsan following a single strong positive Wassermann, only to relapse clinically although the Wassermann remained negative. Had these associations in my experience been unsupported in the literature I should have dismissed them as without significance. Jadassohn, however, refers to Török's observation of positive Wassermanns in association with tuberculids, usually partial positives with one or two antigens. Ravaut, just before the war, had the same experience with several cases in which syphilis could apparently be excluded. Snow and Cooper, as a result of the study of the Wassermann in an army tuberculosis sanitarium, conclude that partial positives in tuberculosis do occur in the absence of syphilis and that they may be due to the cholesterin in cholesterinized antigens. Petroff regards these observations as fully confirmed. My own clinical observations on this point are recorded without further comment, since it is impossible to generalize on so small a group of

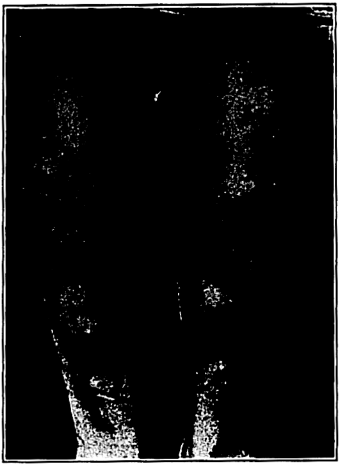

FIG. 17 (174923).—Scarring of a rather large papulonecrotic tuberculid on the calf of the leg. Note the multiplicity of lesions, lack of configuration, peripheral hyperpigmentation. Patient with tuberculous adenitis and arthritic symptoms.

cases. In view of these observations it behooves the clinician to give a second thought to the positive Wassermann in association with a tuberculid before accepting it as evidence of syphilis. The caution with reference to the therapeutic test in this connection (p. 325) should also be recalled.

Certain other evidence of an allergic instability in patients with tuberculids appeared in the course of the salvarsan treatment of the patients, and will be discussed in another paper. Of 18 cases on which data are available, 9, or 50 per cent., showed varying degrees of idiosyncrasy to arsphenamin or neoarsphenamin. Four reacted acutely, by nitritoid crises on the table, two of them repeatedly. One had a delayed reaction with a toxic erythema, three had gastro-intestinal reactions repeatedly and one ran temperatures after injections. This percentage of reactivity enormously exceeds the average observed in patients on the dermatologic service and points to a marked intolerance or instability.

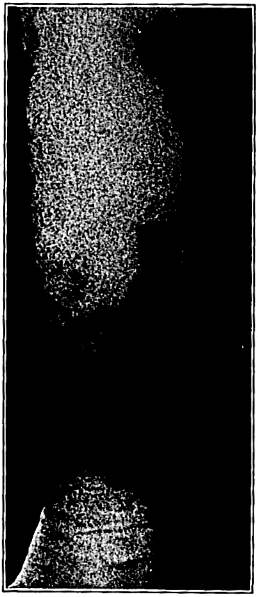

FIG. 18 (212370).—Hyperpigmentation and scarring due to papulonecrotic lesions on a stasis leg. Patient also had folliclis on the fingers.

The importance of doing tuberculin reactions in all cases was not appreciated until the evidence of allergic peculiarities began to appear. They were, therefore, done in only 6, by the von Pirquet method. Three active cases were positive and 3 less active cases were negative. The results of tuberculin therapy will be summarized in a subsequent paper. No conclusions should be drawn from the results mentioned here.

Allergy and the Interpretation of the Secondary Focus in Tuberculids. It should be understood that no attempt is made to consider either the existence or the importance of a secondary pyogenic focus in cases exhibiting tuberculids, as demonstrated by so small a series as 30 cases. None the less the material studied strongly suggests such a factor. Whether a seemingly pyogenic focal disturbance such as erythema nodosum is a forerunner of tuberculosis as suggested in 1907 by Abt, and as mentioned by Jadassohn in 1915, or merely a follower, remains undecided. It is, of course conceivable on the one hand that a co-existent source of pyogenic infection prepares the soil for tuberculosis much as measles increases the susceptibility to the disease. On the other hand, a tuberculous infection may prepare the soil for the pyogenic. Cases in this series suggest that such extirpation of the pyogenic focus as can be accomplished clinically does not substantially alter the picture so long as the tuberculous focus remains active. The latter is therefore probably the direct etiologic agent. I have suggested theoretical possibilities relating the pyogenic secondary focus to the production of the cutaneous hypersusceptibility which underlies the pathology of a tuberculid in the hope of stimulating experimental study of a possible association between the two as well as further observation on the clinical existence or non-existence of such an entity. A certain amount of clinical evidence for the ability of a focus of pyogenic infection to produce allergic phenomena in the skin in the form of dermatitides and urticarias is apparently accumulating. The subject of the etiologic relation of focal infection to skin diseases is still so completely in its beginnings, however, that clinical observations can hope as yet to have only suggestive value.

SUMMARY.

1. The material of this study consists of thirty cases of the so-called papulonecrotic tuberculid, of erythema induratum, and of associated conditions constituting, according to the most widely accepted explanation, the allergic response of a hypersensitized skin to emboli of tubercle bacilli from a tuberculous focus elsewhere in the body.

2. Internists and general diagnosticians should find it worth while to familiarize themselves with the essential lesion of these

types of tuberculids, which may prove of great assistance in the recognition of obscure tuberculosis.

3. The tuberculid when not ignored by the general diagnostician is usually confused as shown by this series, with acne and furunculosis, with syphilis, especially if the Wassermann is positive, and on the legs, with acute surgical conditions and ulcus varicosus. Therapeutic tests for syphilis with arsphenamine are misleading in these cases. The diagnostic import of the lesions in obscure lymphadenitis was at times overlooked.

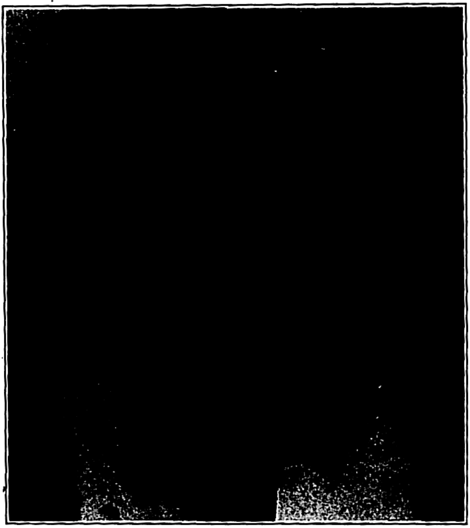

FIG. 19 (197425).—Scar of a healed ulcer, plaque of erythema induratum on the lower portion of the calf.

4. Association with tuberculosis in this series was evidenced by a family history in one-fourth of the cases, incontestible objective signs in more than half (57 per cent.), and presumptive signs of the disease in 70 per cent. One-third of the patients had radiographic signs of pulmonary tuberculosis; an equal number had suggestive or positive physical signs of lung involvement. The importance of lymphatic involvement is illustrated by the fact that two-thirds of them had a tuberculous lymphadenitis.

5. The type and location of the focus of tuberculosis do not seem to influence the tuberculid beyond the marked association with glandular involvement. On the other hand, the influence of vascular

abnormalities and chronic passive congestion in the extremities is very apparent. Ninety-six per cent. of the lesions involved the extremities. Lesions appeared on the ear in 13 per cent.

6. Slight fever at onset, loss of weight in 40 per cent., amenorrhea in 43 per cent. of the women, moderate leukopenia, slight but occasionally severe anemia, and vernal periodicity are the significant signs. An onset and course marked by rheumatic symptoms is very common (46 per cent.) and often misinterpreted. The recognition of the focus of tuberculosis must depend largely upon objective evidence. There is a notable absence of cough, sweats and hemoptysis. Florid, seemingly robust types of patients are not infrequently subjects of tuberculids.

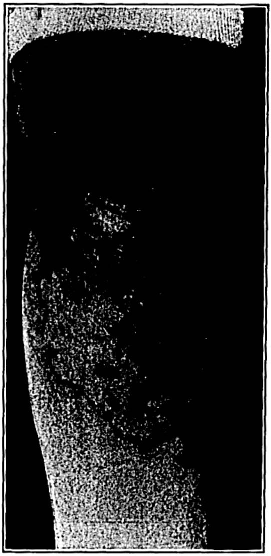

FIG. 20 (218126).—Scar of a noduloulcerative syphilid of the pretibial region. Note the arciform, polycyclic configuration.

7. Evidence of the importance of a septic focus and collateral types of infections appears from the history of tonsillitis in 39 per cent., "rheumatism" in 46 per cent., pneumonia in 26 per cent., grippe in 54 per cent. and pleurisy in 18 per cent. These conditions seemed frequently to stand in direct predisposing or exciting relation to the tuberculid. A total of 70 per cent. had symptoms and

findings suggesting the presence of a septic focus, and 62 per cent. had had significant respiratory infections excluding pleurisy.

8. While no direct relation of the tuberculid to the clinical condition of the tonsils could be established, 50 per cent. of the patients had markedly septic tonsils, the remainder were passable, and none were normal.

9. Examination of the teeth by x-ray in a limited number of the later cases demonstrated the presence of septic foci in 45 per cent. of nine patients. Other foci should be searched for.

10. While the secondary or septic focus was obviously present its influence is obscure. Removal of the tonsils in seven cases failed to prevent the outbreak of a tuberculid or modify its course, and complete extirpation of all recognizable septic foci in two cases, without removing or treating the tuberculous focus, was also unavailing.

11. It is conceivable that the effect of a secondary septic focus, while not direct, is predisposing in that toxins or even bacteria, emanating from it may be in part responsible for the cutaneous allergy which is presupposed in explaining the pathogenesis of the papulonecrotic tuberculid. Evidences of the ability of a septic focus to produce or predispose to dermatitis, urticaria and similar expressions of cutaneous hyperirritability are accumulating. Further indirect evidence of a possible peculiar allergic state of patients with tuberculids is found in reported and personally observed cases of non-specificity in their Wassermann reactions and in their hypersusceptibility to arsphenamin.

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STUDIES IN A CASE OF ACUTE BICHLORIDE OF MERCURY POISONING TREATED BY THE NEWER METHODS, AND FOLLOWED BY RECOVERY.

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1. INTRODUCTION AND REVIEW OF THE LITERATURE. In recent years the treatment of the formerly hopeless cases of bichloride of mercury poisoning has developed along new lines that seem to be of great promise as regards the recovery of these cases.

Lieb and Goodwin[1] emphasized the importance of repeated gastric lavage to remove the mercury excreted into the stomach and Lambert and Patterson[2] have shown the necessity of utilizing every means we have for the purpose of elimination of the mercury from the body. They have shown the necessity of frequent gastric lavage and colon irrigations continued until the washings are free from mercury when tested chemically. Other workers have advised procedures some of which when studied experimentally have failed to protect against mercury poisoning.

Hall[3] recommended the use of a solution of potassium iodide, quinine hydrochloride, hydrochloric acid and water, but Barbour[4] and also Sansum[5] have shown that this antidote is valueless. Fantus[6] has shown that the use of egg albumen is without value unless

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[1] Jour. Am. Med. Assn., 1915, lxiv, 2041.

[2] Arch. Int. Med., 1915, xvi, 865.

[3] Jour. Am. Pharm. Assn., 1915, iii, 182.

[4] Jour. Am. Med. Assn., 1915, lxiv, 736.

[5] Ibid., 1918, lxx, 824.

[6] Jour. Lab. and Clin. Med., 1916, i, 879; 1917, ii, 813.